CRD summary
This review concluded that methylene-blue chromoendoscopy targeted biopsies and conventional random biopsies were comparable in the detection of specialised intestinal metaplasia and dysplasia in patients with Barrett’s oesophagus. Given the limitations with the included studies, difficulties in determining the quality of the studies, and the potential for bias in the review, the authors' conclusions should be interpreted with caution.

Authors' objectives
To compare the diagnostic yield of methylene-blue chromoendoscopy targeted biopsy with the conventional four-quadrant random biopsy in the detection of specialised intestinal metaplasia and dysplasia in patients with Barrett's oesophagus.

Searching
MEDLINE, EMBASE, and Cochrane Central Register of Controlled Trials (CENTRAL) were searched from 1980 to October 2007 with no language restrictions. Search terms were reported. In addition, reference citations and bibliographies of retrieved articles were manually searched, as well as abstracts presented at the proceedings of Digestive Disease Week and the meetings of the American College of Gastroenterology (2002 to 2007).

Study selection
Prospective studies comparing methylene-blue chromoendoscopy targeted biopsy with conventional four-quadrant random biopsy, in patients with histopathologically confirmed lesions, were eligible for inclusion. Eligible studies were required to perform procedures successively on each patient, under comparable conditions, and to report the diagnostic yield of specialised intestinal metaplasia and various grades of dysplasia in patients with Barrett's oesophagus. Clinical reviews, editorials, and brief communications/letters were excluded from the review.

Included studies were conducted in the USA, UK, Germany, Brazil and Turkey, and were of patients with long- or short-segment Barrett's oesophagus. The majority of studies used standard methylene-blue biopsy technique (biopsy of both methylene-blue stained and unstained mucosa). Methylene-blue 0.5% concentration was administered during the methylene-blue staining process; contact time was two minutes in the majority of studies.

Two reviewers independently screened studies for inclusion. Disagreements were resolved through consultation with a third reviewer; where necessary, further information was requested from the study authors.

Assessment of study quality
The authors stated that studies were defined as being of high quality if they were blinded and were reported in full, but no other details were provided.

Data extraction
Data on the diagnostic yield of specialised intestinal metaplasia and dysplasia were extracted to calculate incremental yield and 95% confidence intervals (CIs).

The authors did not state how many reviewers performed the data extraction.

Methods of synthesis
Weighted incremental yields and their 95% CIs were pooled using a fixed-effects model, or a random-effects model where there was evidence of statistical heterogeneity. The authors stated that the number needed to test for one positive finding was also calculated, but no data were reported. Subgroup analyses were performed to assess
diagnostic yield in patients with low-grade dysplasia and high-grade dysplasia and/or oesophageal adenocarcinoma.

Statistical heterogeneity was assessed using the $X^2$ and $I^2$ tests. Potential sources of statistical heterogeneity, including methylene-blue chromoendoscopy concentration, contact time, and biopsy technique, were investigated. Sensitivity analysis was carried out using only studies of the highest quality. Funnel plots were used to assess publication bias in studies detecting high-grade dysplasia and/or oesophageal adenocarcinoma.

**Results of the review**

Nine studies (n=450 patients) were included in the review; 164 patients with short-segment Barrett's oesophagus; 256 patients with long segment (eight studies). Sample sizes ranged between 30 and 86 patients. Seven studies were blinded.

There were no significant differences between methylene-blue chromoendoscopy and random biopsy in the detection of specialised intestinal metaplasia (p=0.44; six studies) or the detection of dysplasia (p=0.08; nine studies). There were no significant differences between the two procedures for the detection of low-grade dysplasia (p=0.17; eight studies) or high-grade dysplasia and/or oesophageal adenocarcinoma (p=0.11; eight studies). There was evidence of statistical heterogeneity for all comparisons. Sensitivity analyses did not significantly alter the results.

There was no evidence of publication bias in studies detecting high-grade dysplasia and/or oesophageal adenocarcinoma.

**Authors’ conclusions**

Methylene-blue chromoendoscopy targeted biopsies provided no benefit compared with random biopsy in the detection of specialised intestinal metaplasia and dysplasia during endoscopic evaluation of patients with Barrett's oesophagus.

**CRD commentary**

The review question was clear and was supported by appropriate inclusion criteria for participants, interventions, comparators and outcomes. Inclusion criteria for study design were broad. Several appropriate sources were searched for relevant articles with no language restrictions, which reduced the potential for language bias. There was no apparent attempt to locate unpublished articles, so potentially relevant articles may have been missed. Publication bias was assessed for certain grades of dysplasia and no bias was detected. The authors attempted to reduce reviewer error and bias during study selection by undertaking this stage in duplicate. However, the same was not true for validity assessment and data extraction, so reviewer error and bias could not be completely ruled out.

Although the authors included study quality as part of the data synthesis, the validity assessment was very limited, so it was difficult to determine the quality of the studies. The authors acknowledged certain limitations with the included studies, such as small sample sizes and potential for clinical and methodological heterogeneity.

Given the limitations with the included studies, difficulties in determining the quality of the studies, and the potential for bias in the review, the authors’ conclusions should be interpreted with caution.

**Implications of the review for practice and research**

**Practice**: The authors did not state any implications for practice.

**Research**: The authors stated that further well-designed, randomised trials of conventional or electronic chromoendoscopy, with adequate samples sizes, are required.

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